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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/944,175	09/04/2001	Nobuhiko Ogura	Q65952	9850

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,175	OGURA, NOBUHIKO	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8 and 10-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 10-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application and Claims Status

1. Applicants' amendment and response filed 01/18/2006 are acknowledged and entered.

2. Claims 1, 2, 4-8, and 10-22 were pending. Applicants have amended claim 1. No claims were added or canceled. Therefore, claims 1, 2, 4-8, and 10-22 are currently pending and are under consideration in this Office Action.

Withdrawn Objection(s) and /or Rejection(s)

3. All rejections are withdrawn in view of Applicants' arguments and/or amendments wherein the "*combined bodies of the probe and the captured target*" are fractioned, i.e. the complex of probe and target is "electrophoresed".

New Objection(s) and /or Rejection(s)

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 4-8, and 10-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of analyzing biochemical wherein the steps of a) fixing the probes on a substrate, i.e. a "non-covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex

of both the probe and capture target are "separated" from the substrate (see instant specification pg. 21-23 and 40-43), does not reasonably provide enablement for the method of analyzing biochemical wherein the steps of a) fixing the probes on a substrate, i.e. "covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate. In addition the instant specification does not provide a specific definition for the step of fixing the probes on a substrate such that the broadest reasonable interpretation, i.e. the scope of this step, of this step would include both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a scope of enablement rejection (see MPEP § 2164.08 and *In re* Goodman, 11 F.3d 1046, 1052, 29 USPQ2d 2010, 2015 (Fed. Cir. 1993)).

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to: 1) The breadth of the claims; 2) The nature of the invention; 3) The state of the prior art; 4) The level of one of ordinary skill; 5) The level of predictability in the art; 6) The amount of direction provided by the inventor; 7) The presence or absence of working examples; and 8) The quantity of experimentation necessary needed to make or use the invention based on the disclosure. (See *In re Wands* USPQ 2d 1400 (CAFC 1988)).

(1-2) The breadth of the claims and the nature of the invention:

The instant claimed invention recites a biochemical analyzing method. The method comprise the steps of 1) fixing probes selected in advance on a substrate; 2) binding a target with the probes using a specific binding reaction to capture the target; 3) fractionating combined bodies of the probe and the captured target; 4) detecting only a fractionated target; and 5) quantitatively analyzing the detected target. Wherein the probes are spotted on the substrate and fixed thereon, and the combined bodies of the probe and the captured targets are electrophoresed, thereby being fractionated, wherein during the fractionating, the combined bodies of the probe and the captured target is separated into a plurality of fractions based on molecular weight.

As claimed, the method scope would include both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate such that the instant specification does not reasonably provide enablement for the method of analyzing biochemical wherein the steps of a) fixing the probes on a substrate, i.e. "covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate. Since the instant specification does not provide a specific definition for the step of fixing the probes on a substrate, the broadest reasonable interpretation, i.e. the scope of step (1), would include both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate.

(3 and 5) The state of the prior art and the level of predictability in the art:

The present invention relates affinity electrophoresis. Affinity electrophoresis includes both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate. For the affinity electrophoresis in which the probe is "covalently"

attached to the substrate, the complex of probe and target are retarded and does not migrate, i.e. fractionating. Muscate et al. disclose the method of capillary affinity gel electrophoresis (*Anal. Chem.*, **1998**, 70(7), pgs. 1419-1424)(see Abstract; pg. 1419, left col. lines 1-10; left col., line 47 thru right col., line 7). The method comprises the steps of a) covalently immobilized onto the polymer backbone, i.e. the substrate, the complementary sequence of the target oligonucleotide; b) the sample containing the target oligonucleotide electrophoresed; c) hybridizing the target oligonucleotide to the complementary sequence of the target oligonucleotide that is covalently immobilized on the polymer backbone wherein the complementary sequence of the target oligonucleotide retard the migration of the target oligonucleotide and the unmatched oligonucleotide continue to migrate through the polymer network; and d) releasing the hybridized target oligonucleotide via changing the temperature (see pg. 1421, right col., lines 29-46; pg. 1422, fig. 2). In addition, Muscate et al. also disclose that in known affinity electrophoresis in which the probe is "covalently" attached to the substrate, the complex of probe and target are retarded and does not migrate, i.e. fractionating (see pg. 1420, left col., lines 13-19). Consequently, the scope of the method as claimed include the steps of "covalent attachment" of the probe onto the substrate and the migration of the complex of probe and target, i.e. fractionating, which has yet to be identified by the specification and the state of the art.

(4) The level of one of ordinary skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples.

Since the instant specification does not provide a specific definition for the step of fixing the probes on a substrate, the broadest reasonable interpretation, i.e. the scope of the fixing step, would include both "non-covalent attachment" of the probe onto the substrate and "covalent attachment" of the probe onto the substrate. The instant specification description is directed to the method comprising the steps of a) spotting and fixing the probe onto the substrate; b) hybridizing the target to the probe; and c) transferring the complex of probe and target, i.e. the combined bodies of probe and target, onto a gel via electrophoresis, i.e. the complex of probe and target are migrated to the gel and separated base on their size (see instant specification pg. 21-23 and 40-43). Base on this disclosure, the specification is only enable for the method of analyzing biochemical wherein the steps of a) fixing the probes on a substrate, i.e. a "non-covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate. Moreover, the specification does not provide any working examples.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

Accordingly, the claims are broad in scope with regard to the claimed method that include the steps of a) fixing the probes on a substrate, i.e. "covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate and the lack of specification guidance as how the complex of probe and target can be migrated, i.e. fractionated, by electrophoresis when the probe is "covalently" attached to the substrate such that it would

necessarily result in undue experimentation for one of ordinary skill wishing to practice the presently claimed invention.

Therefore based on the evidences as a whole regarding each of the above factors (e.g. factors 1-8), the specification, at the time the application was filed, does not satisfy the enablement requirement for the claimed method that include the steps of a) fixing the probes on a substrate, i.e. "covalent attachment" of the probe onto the substrate, and b) fractionating combined bodies of the probe and capture target, i.e. the complex of both the probe and capture target are "separated" from the substrate.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 4-8, and 10-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 is vague and indefinite because there is no correlation between the products that result in the method step of binding a target with the probes using a specific binding reaction to capture the target and the limitation of "*the combined bodies of the probe and the captured target are separated into a plurality of fractions based on molecular weight*". That is the products produced from the method step of binding a target with the probes using a specific binding reaction are a multiplicity of one 'type' of probe and target complexes, but the limitation of "*the combined bodies of the probe and*

the captured target are separated into a plurality of fractions based on molecular weight" imply that a plurality of different 'types' of probe and target complexes are formed such that they are separated based on molecular weight. Therefore, claim 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

b. Claims 4-7 and 15 recite the limitation "respective captured targets". There is insufficient antecedent basis for this limitation in claim 1. It is suggested that this limitation is amended to "*combined bodies of the probe and the captured target*" or "combined bodies". Therefore, claims 4-7, 15, and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

c. Claim 21 recites the limitation of "targets". There is insufficient antecedent basis for this limitation in claim 1. It is suggested that this limitation is amended to "*combined bodies of the probe and the captured target*" or "combined bodies". Therefore, claim 21 is rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 2, 5, 11, 13, 15, 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishii et al. (*Nucleic Acids Res.*, **1997**, 25(17), pgs. 3550-3551).

Note: The instant claimed method step of fixing probes selected in advance on a substrate is interpreted as "non-covalent attachment" of the probes onto the substrate.

For claims 1, 2, 5, 11, 19, and 22, Ishii et al. disclose a method for selecting monoclonal antibodies (mAb) against DNA-binding protein complex (see Abstract; pg. 3550, left col., line 17 thru right col., line 5). The method comprises the steps of a) fixing probes in advance on a substrate (see e.g. pg. 3550, left col., lines 17-21 wherein mAb are "selected in advanced" using hybridoma technology and are fixed onto a 96-well plate (refers to instant claim 11); pg. 3551, fig. 1(a); pg. 3551, fig. 1(b) showing the mAb ligands were "fixed" on the substrate using anti Ig(Fc)Ab (refers to instant claimed limitation of the probes are spotted on the substrate and fixed thereon); b) binding a target with the probes using specific binding reaction to capture the target (see e.g. pg. 3550, left col., lines 21-24; pg. 3551, fig. 1(a) wherein an antigen target is bound using specific antigen-antibody reaction (refers to instant claim 2)); c) fractionating combined bodies of the probe and the captured target (see e.g. pg. 3550, left col., line 31 thru right col., line 5; pg. 3551, fig. 1(b) showing the electromobility shift assay (refers to instant claim 5); pg. 3551, fig. 2(b) showing supershift of mAb/Rbf1p complex); d) detecting only a fractionated target (see e.g. pg. 3551, fig. 2(b) showing supershift for mAb against Rbf1p); and e) quantitatively analyzing the detected target (see e.g. pg. 3551, fig. 1(b) caption describing that the radioactivity of the complex is quantified by an image analyzer (refers to instant claim 19); pg. 3551, fig. 1(b) graph of competition activity percentage; pg. 3551, fig. 2(b) showing dye intensity analysis). In addition, Ishii et al. disclose that during fractionation, the combined bodies of probe and the captured target is separated into plurality of fractions base on molecular weight (see e.g. pg. 3551, fig. 1(a) showing the electromobility shift assay (refers to instant claimed limitation of the combined bodies of the probe and the captured targets are electrophoresed, thereby being

fractionated); pg. 3551, fig. 2(b) showing bands of supershift and free that have been fractionated based on molecular weight (refers to claim 22)).

For claims 13 and 15, Ishii et al. disclose the step of labeling the target with a fluorescence substance after binding reaction (see e.g. pg. 3550, left col., lines 21-24 wherein the target is labeled with horseradish peroxidase; pg. 3551, fig. 1(a)).

Therefore, the method of Ishii et al. anticipates the presently claimed invention.

Conclusion

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
April 3, 2006

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